DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention
Atlanta GA 30333

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Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane
Rockville, Maryland 20852

RE: Docket No. 2001D-0044: Draft Guidance for CLIA Waiver Applications

The Division of HIV/AIDS Prevention (DHAP), National Center for HIV, STD, and TB Prevention, would like to comment on the Draft Guidance for CLIA Waiver Applications. These comments are based on our experience with deliberations over two rapid HIV tests that were recently waived and our data from post marketing surveillance of these waived devices. DHAP believes that several provisions in the draft guidance will have an adverse effect on the availability of important diagnostic devices and, as a result, on public health.

1. Page 8, bullet 9: The requirement for a simple test to provide "instructions and materials for obtaining and shipping specimens for confirmation testing" is unwarranted and will be burdensome. For low prevalence conditions where only 1% to 5% of persons might need confirmation, including materials for confirmatory testing with all kits would cause an unnecessary increase in cost and disposable waste. We strongly suggest this language be changed to "instructions for confirmatory testing."

2. Page 8, paragraph 2, bullet 3: DHAP strongly opposes precluding waiver of tests for reportable conditions by defining that such tests are not simple. Reportability of the health condition has nothing to do with the test's simplicity. As steward of the nation's public health surveillance, CDC recognizes the importance of surveillance, but also the significant limitations of passive reporting. DHAP has long endorsed activities that enhance detection, even if at the expense of reporting. For example, CDC supports anonymous testing for HIV because some persons would avoid testing if their name were to be reported. Post marketing information for waived HIV tests (which would have been precluded under the proposed provision) indicates increased access, availability, utilization, and receipt of results with waived, point-of-care HIV tests. Data for the waived rapid influenza diagnostic test also showed that access to this waived test, in fact, improved public health surveillance for influenza virus (Effler et al, Emerging Infectious Diseases, 8:23-28, January 2002). Precluding waiver of tests for reportable diseases, especially tests for sexually transmitted diseases, would pose a significant barrier for prevention and control efforts. There is no scientific or epidemiologic basis for such a requirement.

3. Page 26, paragraph 1-2: Although DHAP agrees that the ability to correctly obtain samples from patients should be evaluated as part of waiver studies, the requirement to conduct waiver studies using only patient samples is unreasonable for low prevalence conditions such as HIV or syphilis.

The proposed guidance states that 120 positive and 120 negative samples should be obtained from patients at sites representative of the intended patient population. However, no more than 10% of specimens can be artificially constructed or archival. For HIV, it is difficult to locate clinic populations with prevalence as high as 2% to 5%. Therefore, obtaining the 108 positive samples required for the CLIA waiver study would require testing 2,000 to 6,000 patients. This is a larger trial than that required for PMA approval. The expense would likely discourage many product sponsors, and eventually result in a considerably increased cost for the waived product. It also places an undue burden on the large number of human subjects – most of whom are negative - who would need to be tested twice as part of the trial.

4. Page 27, Section C2b. The recommended study design for determining qualitative device performance near the clinical cutoff proposes an inappropriate comparison (aliquots of samples that are near the cutoff as determined only by the comparison method [CM]). In the case of HIV and several other point of care tests with visually read end points, the comparison method is quantitative. Several studies have documented that the procedures recommended in the guidance (pooling or diluting samples to create sufficient material for 60 aliquots) can interfere with the performance of FDA-approved tests (see Weiblen et al, Boston Biomedica; Yen-Lieberman et al, Cleveland Clinic). This phenomenon has posed numerous difficulties for preparing specimens for proficiency panels. Given that a waiver application cannot be initiated until a device has been approved for use by professional operators, the sensitivity near the cutoff of the device itself has already been determined. Therefore, it is essential that the weak positive specimens to be tested in waiver studies should be those that are determined by professional operators to be weak positive on the waived method (WM), not the CM.

5. Page 29-30. The Quality Control Labeling Recommendations stating the instructions should "emphasize the value of external control testing at regular intervals for ensuring operator competency" exceeds the requirements in 42 CFR Part 493 for CLIA-waived tests (for which proficiency testing is not required) and also the recommendations developed by a CDC-sponsored expert panel for quality assurance of waived testing. Periodic testing of external controls is one method for ensuring operator competency, but it has proven to be expensive (consuming controls and extra test devices) and acceptable alternatives exist. Thus, it seems inappropriate to recommend emphasis on this one method.

Thank you for your consideration of these comments. We would be glad to discuss any of these items with you.

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